REMARKS

Reconsideration of this application is respectfully requested.

IDS

Applicants submit herewith an IDS listing three additional references. Any inconvenience to the Examiner is sincerely regretted.

STATUS OF THE CLAIMS

Following entry of this Amendment, claims 3, 4, and 15-32 will be pending. Claims 3 and 15 are amended. Claims 1, 2, and 5-14 are cancelled. Claims 16-32 are added.

Support for the new and amended claims is as follows:

Claim 3: page 11, line 22; page 3, lines 8-13.

Claims 16-26: page 11, line 23-25, and page 3, lines 8-13.

Claims 27-32: page 13, line 5; page 3, lines 8-13.

No extra claims fees are believed owed as a result of the added claims, but the Commissioner is authorized to charge the above-mentioned deposit account the required amount in the event that this is incorrect.

INFORMALITIES

The informalities referred to at page 2 of the action will be addressed once an indication of allowability is obtained. A new declaration will be submitted to address the objection to incorporation by reference at page 1.

Claims 3-4 and 15 are objected to as dependent on non-elected claim 1. They have been amended so that claim 3 is independent, and all claims ultimately depend from claim 3.

Claim 15 has been amended to depend from only one claim.

REJECTION UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claims 3-4 and 15 stand rejected under 35 U.S.C. §112, second paragraph as indefinite.

The claims no longer recite a disintegrin domain or stringent conditions. Therefore, withdrawal of the rejection is requested.

REJECTION UNDER 35 U.S.C. §112, FIRST PARAGRAPH

Claims 3-4 and 15 stand rejected under 35 U.S.C. §112, first paragraph for lack of enablement. The primary basis for the rejection appears to be that the claims relate to a large genus of peptides, including those that are only 80% identical to seq id 2, and those that are encoded by nucleic acids that hybridize with short stretches of nucleic acids encoding portions of the newly found amino acid sequence.

The claims have been amended in a way that is believed to address the bases of the Examiner's rejection. Specifically, language relating to 80% identity has been replaced with language requiring at least 90% identity to the disclosed amino acid sequences for the metalloproteinase domain and prodomain. Language relating to amino acid sequences encoded by very short nucleotide sequences has been deleted.

In view of the amendments to the claims, withdrawal of the rejection of claims 3-4 and 15 under 35 U.S.C. §112, first paragraph for lack of enablement is respectfully requested.

The Examiner has also rejected claims 3 and 15 as lacking written description. The claims have been amended so that, it is submitted, they encompass a substantially narrower range of species that are easily envisioned by one skilled in this art. The scope of claims is such, it is submitted, that the functional characteristics of the invention are supported by applicants' disclosure of the sequences shown, and activities of the particular domains described. Therefore, withdrawal of the rejection on this basis is respectfully requested.

REJECTION S UNDER 35 U.S.C. §102(a)

Claim 3 stands rejected under 35 U.S.C. §102(a) as anticipated by Nagase et al., GenBank Accession No. AB037733.

This rejection is based on the disclosure in GenBank of a sequence similar to applicants.

It is applicants' understanding that the GenBank sequences can be updated, and that the content of the original sequence may not be readily apparent from inspection of the database.

In this case, applicants believe that they were first to discover the metalloproteinase domain and prodomain sequences of this aggrecanase. It is respectfully submitted that the listing in GenBank is insufficient evidence to show the disclosure as of the date shown, in view of uncertainty as to when and how the sequence may have been updated.

Withdrawal of the rejection of claims 3-4 as anticipated by Nagase et al. is respectfully requested.

Claims 3 and 15 stand rejected as anticipated by US Patent 5,733,771. This rejection is based on inclusion in applicants' claim scope of amino acid sequences encoded by very short nucleotide sequences. The amended claims are limited to longer sequences. Withdrawal of the rejection is therefore requested.

CONCLUSION

This application is submitted to now be in condition for allowance. Issuance of a notice to that effect is respectfully requested.

Respectfully submitted,

Dated:_____

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VERSION OF CLAIMS SHOWING CHANGES
DO NOT ENTER

Cancel claims 1-2 and 5-14.

Amend claim 3 as follows:

3. (Amended) A polypeptide having an amino acid sequence comprising an amino acid sequence [encoded by the isolated polynucleotide molecule of claim 1] having at least 90% identity to the amino acid sequence of the metalloproteinase domain or the prodomain of SEQ ID NO 2.

15. (Amended) A pharmaceutical composition for the treatment of arthritis [(osteoarthritis and rheumatoid arthritis)], inflammatory bowel disease, Crohn's disease, emphysema, acute respiratory distress syndrome, asthma, chronic obstructive pulmonary disease, Alzheimer's disease, organ transplant toxicity and rejection, cachexia, allergy, cancer [(such as solid tumor cancer including colon, breast, lung, prostate, brain and hematopoietic malignancies including leukemia and lymphoma)], tissue ulcerations, restenosis, periodontal disease, epidermolysis bullosa, osteoporosis, loosening of artificial joints implants, atherosclerosis [(including atherosclerotic plaque rupture)], aortic aneurysm [(including abdominal aortic and brain aortic aneurysm)], congestive heart failure, myocardial infarction, stroke, cerebral ischemia, head trauma, spinal cord injury, neurodegenerative diseases [(acute and chronic)], autoimmune disorders, Huntington's disease, Parkinson's disease, migraine, depression, peripheral neuropathy, pain, cerebral amyloid angiopathy, nootropic or cognition enhancement, amyotrophic lateral sclerosis, multiple sclerosis, ocular angiogenesis, corneal injury, macular degeneration, abnormal wound healing, burns, infertility or diabetic shock comprising a therapeutically effective amount of [an agent selected from the group consisting of an agonist or antagonist of ADAMTS-SI,] a polypeptide of claim 3[, and a polynucleotide of claim 1,] in combination with a pharmaceutically acceptable carrier.

Kindly add the following claims:

16. The polypeptide of claim 3 having an amino acid sequence comprising an amino acid sequence having at least 90% identity to the amino acid sequence of the metalloproteinase domain of SEQ ID NO 2.

17. The polypeptide of claim 3 having an amino acid sequence comprising an amino acid sequence having at least 90% identity to the amino acid sequence of the prodomain of SEQ ID NO 2.

18. The polypeptide of claim 3 comprising the amino acid sequence of SEQ ID NO: 2.

19. The polypeptide of claim 3 comprising amino acids 289 to 478 of SEQ ID NO: 2.

20. The polypeptide of claim 3 comprising amino acids 19 to 287 of SEQ ID NO: 2.

21. The polypeptide of claim 3 having an amino acid sequence comprising an amino acid sequence having at least 95% identity to the amino acid sequence of the metalloproteinase domain.

22. The polypeptide of claim 3 having an amino acid sequence comprising an amino acid sequence having at least 95% identity to the amino acid sequence of the prodomain.

23. The polypeptide of claim 3 having an amino acid sequence comprising an amino acid sequence having at least 97% identity to the amino acid sequence of the metalloproteinase domain.

24. The polypeptide of claim 3 having an amino acid sequence comprising an amino acid sequence having at least 97% identity to the amino acid sequence of the prodomain.

25. The polypeptide of claim 3 having an amino acid sequence comprising an amino acid sequence having at least 99% identity to the amino acid sequence of the metalloproteinase domain.

26. The polypeptide of claim 3 having an amino acid sequence comprising an amino acid sequence having at least 99% identity to the amino acid sequence of the prodomain.

27. The polypeptide of claim 22 having 5 to 10 amino acids substituted, deleted, or added, or combinations of such changes.

28. The polypeptide of claim 21 having 1 to 5 amino acids substituted, deleted, or added, or combinations of such changes.

29. The polypeptide of claim 22 having 1 to 5 amino acids substituted, deleted, or added, or combinations of such changes.

30. The polypeptide of claim 21 having 1 amino acid substituted, deleted, or added.

31. The polypeptide of claim 22 having 1 amino acid substituted, deleted, or added.

32. The polypeptide of claim 21 having 1 to 5 conservative amino acid substitutions.